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IMMUNIZATION OF ACUTE LEUKEMIC CHILDREN WITH A LIVE VARICELLA VACCINE (OKA STRAIN)

HITOSHI KAMIYA, TAKASHI KATO, MACHIKO ISAJI, SADAYOSHI TORIGOE, KOICHI OITANI, MASAHIRO ITO, TOSHIAKI IHARA and MINORU SAKURAI

Department of Pediatrics, Mie University School of Medicine, 2-174, Edobashi, Tsu, Mie, 514 Japan

MICHIAKI TAKAHASHI

Research Institute for Microbial Diseases, Osaka University, Suita, Osaka, 565 Japan

A total of 52 acute leukemic children have been safely and effectively vaccinated with live varicella (Oka strain) vaccine given under close clinical and immunological observation. The incidence of zoster in the vaccinated children group was slightly less than that in the group that had experienced natural varicella.

INTRODUCTION

From 1974 to 1976, a live varicella vaccine of the Oka strain. (Takahashi et al., 1974) was used for the first time for 12 leukemic children (Izawa et al., 1977). With careful consideration of the fact that leukemic children are extraordinarily susceptible to VZ virus infection, vaccination was limited to only those children in a good leukemic and immunologic status.

Since that pilot study we have vaccinated a total of 52 children with acute leukemia. This paper reports clinical and immunological observations on these children.

MATERIALS AND METHODS

1. *Vaccine*

The Oka strain of varicella vaccine, which had been passaged in human embryonic lung cells (HEL) 11 times, in guinea pig embryo cells (GPE) 12 times and then in human diploid cells (WI-38) 2 to 9 times, was injected subcutaneously into each patient.

RESULTS

1. *Clinical and serological responses after vaccination*

As shown in Table 1, a total of 52 children with acute leukemia [51 with acute lymphoblastic leukemia (ALL), and 1 with acute myeloblastic leukemia (AML)] were given various doses of vaccine virus. The serological titers and clinical manifestations of 27 of these patients are still under observation and 12 children were followed up for over 5 years.

Seroconversion was observed in all the vaccinees. Ten of the 50 vaccinees showed a clinical reaction; 9 developed rashes, and 4 of these children and one other developed fever, as shown in detail in Table 2. In case 8 (T.M.) the rash lasted for 60 days. However he had no fever, chemotherapy was not discontinued after the appearance of the rash, and this clinical symptoms were not troublesome. In most cases serum antibody titers were measured by

TABLE 1. *Number of vaccinated patients*

Underlying disease	Virus dose (PFU)						Total
	100	200	500	750	1,500	2,500	
Leukemia							52
ALL	12	5	8	21	3	2	51
AML			1				

TABLE 2. *Clinical reactions in vaccinated children with acute leukemia*

Rash

Case	Viral dose (PFU)	Days after vaccination	Number of rashes	Duration of rash (days)
1. H.N	1,500	13	13	2
2. K.O	200	13	30	3
3. T.N	200	21	25	3
4. Y.U	100	24	20	3
5. Y.I	100	9	3	2
6. H.I	500	28	15	2
7. N.Y	750	21	23	3
8. T.N	750	20	100	60[a]
9. M.W	750	23	100	10

Fever

Case	Viral dose	Days after vaccination	Maximum temp. (C)	Duration of fever (days)
1. T.N	200	21	39.0	2
2. Y.U	100	24	39.0	1
3. H.I	500	28	38.3	1
4. Y.M	750	20	39.0	1
5. M.W	750	20	39.0	5

[a] Case 8 received chemotherapy even after appearance of the rash. He had no fever.

TABLE 3. *Eight-year follow-up of neutralizing antibody titers of vaccinated children with acute leukemia*

Years after vaccination	Mean antibody titer	Blood sample	Number of case	Number of seronegative cases
0-1	$2^{2.1}$	108	48	3 (6.3%)
1-3	$2^{2.2}$	84	34	2 (5.9%)
3-5	$2^{2.4}$	41	19	2 (10.5%)
>5	$2^{2.3}$	15	7	0 (9%)

the neutralization test, but some were determined by CF and FAMA tests. The results of follow-ups on the NT antibody titers of the vaccinated children and given in Table 3. The titers of the vaccinated children with acute leukemia persisted well.

2. *Varicella skin reaction in vaccinated children*

Skin reactions against VZ antigen (Kamiya et al., 1977) also became positive after vaccination in most vaccine recipients. The degree of the skin reaction was rather variable during the period of observation depending upon the status of cellular immunity of these children and on their chemotherapeutic treatment. The reaction was definitely positive after cessation of chemotherapy, that is 3 years after initial treatment. The open column in Fig. 1 shows

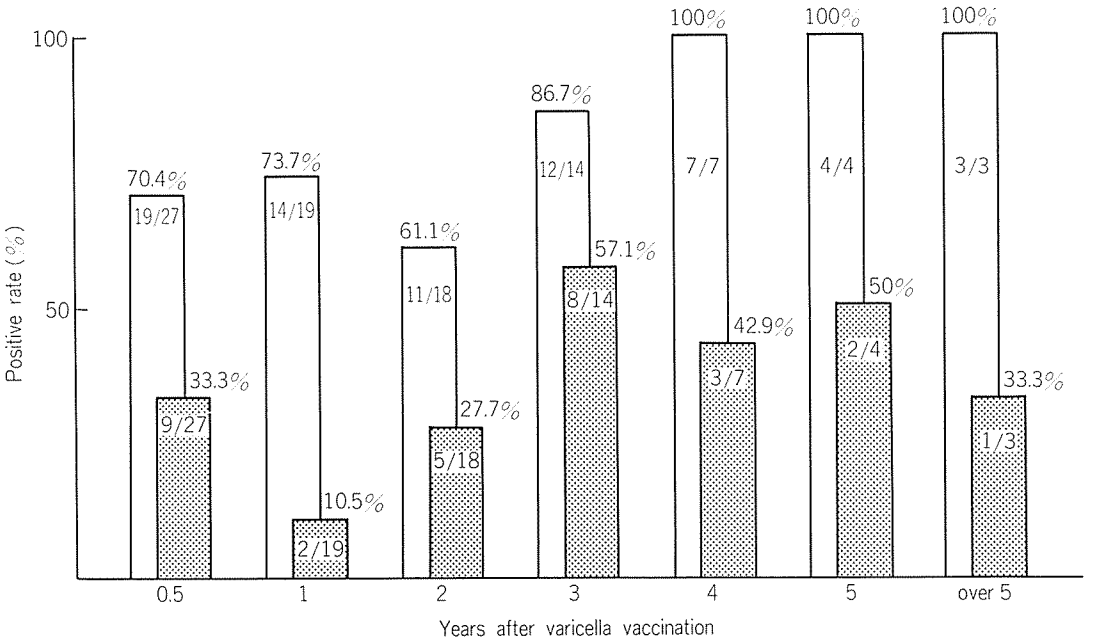

FIGURE 1. Percentage of vaccinated children with leukemia giving positive varicella skin reactions (stippled bars indicate the percentage of children giving a strongly positive reaction).

TABLE 4. *Contact of vaccinated children with varicella patients*

Years after vaccination	Occasions of contact	Kind of contact			Development of clinical varicella
		Family	Playmate	School	
0-0.5	15	5	5	5	0
0.5-1	7	1	3	3	1
1-1.5	4	1	2	1	1
1.5-2	6	0	3	3	0
2-2.5	5	1	1	3	0
>3	8	3	2	3	1
Total	48	11	19	18	3

TABLE 5. *Herpes-zoster in leukemic children*

1) Vaccinees (52 cases)		2) Naturally infected history (63 cases)	
Year after vaccination	No. of cases	Year after infection	No. of cases
<0.5	1	<0.5	1 (1)[b]
0.5-1	2	0.5-1	8 (1)[b]
1 -1.5	0	1 -1.5	0
1.5-2	3 (1)[a]	1.5-2	0
2 -2.5	0	2 -2.5	1
1.5-3	0	2.5-3	0
>3	2 (1)[a]	>3	1
Total	8	Total	11
Rate	15.4%	Rate	12.5%

[a,b] The same patient developed zoster twice.

the percentage of cases giving more than one positive reaction (erythematous change of 5–10 mm in diameter) and the stippled column shows the percentage of those giving two positive reactions of more than 10 mm in diameter.

3. *Protective effect of vaccination against contact infection*

The efficacy of the vaccine was also judged by whether vaccinated patients developed clinical manifestation after exposure to cases of varicella. As shown in Table 4, among a total of 48 exposures of vaccinees to natural infection, only 3 children (2 family, 1 classmate) developed clinical varicella and clinical symptoms were mild (20–30 rashes and fever for one day), suggesting that the immunity induced by vaccination was effective in reducing their symptoms.

4. *Incidence of zoster in vaccinated children*

Table 5 shows a comparison of the incidences of zoster in the vaccinated leukemic children and in children who had experienced natural varicella infection. Both groups had received the same kind of chemotherapy. There were 8 cases of zoster among 52 vaccinated children (15.4%) and among 63 children after natural varicella infection (17.5%).

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